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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,246	12/13/2000	Peter S. Lu	020054000311	8356

20350 7590 08/14/2002

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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/14/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,246	LU ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *5,16-29 and 31-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-15 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-37* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments of 20 September 2001 (Paper No. 6) and 24 April 2002 (Paper No. 13) have been entered in full. Claims 1, 4, 12-13 and 30 are amended.

Election/Restrictions

Applicant's election without traverse of Group A, claims 1-4, 6-15, and 30, drawn to an isolated CLASP-3 polynucleotide, expression vector, host cell, and method of producing a CLASP-3 polypeptide in Paper No. 12 (19 March 2002) is acknowledged.

Claims 5, 16-29, and 31-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12 (19 March 2002).

Claims 1-4, 6-15, and 30 are under consideration in the instant application.

Priority

1. It is noted that this application appears to claim subject matter disclosed in prior copending Application No. 09/687,837, filed 13 October 2000. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

2. Furthermore, the proper priority cannot be completely determined because the first paragraph of the specification and the declaration are inconsistent. For example, the declaration does not claim priority under 35 U.S.C. § 119(e) to 60/240,503 (10/13/2000), 60/162,498

(10/29/2000), and 60/160,860 (10/21/1999), which are mentioned in the first line of the specification. If Applicant intends to claim priority to these applications, a new oath or declaration in compliance with 37 CFR 1.67(a) identifying these applications by application number and filing date is required. See MPEP §§ 602.01 and 602.02. Otherwise, these applications must be deleted from the first line of the specification.

Sequence Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the KIAA0716 sequence disclosed in Figure 3B is not accompanied by the required reference to the relevant sequence identifier.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Specification

4. The disclosure is objected to because of the following informalities:

4a. Patent applications are referenced throughout the disclosure (pg 2, line 7; pg 119, line 28; pg 32, lines 19-29). The status of the applications must be updated.

4b. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (See page 13, line 5). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4c. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "NUCLEIC ACID MOLECULE ENCODING A CLASP-3 TRANSMEMBRANE PROTEIN".

Appropriate correction is required.

Claim Objections

5. Claim 1 is objected to because of the following informalities:

5a. Claim 1(c) at line 3 is missing the term "least" before the phrase "25 contiguous residues".

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 6-15, and 30 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

Specifically, claims 1-4, 6-15, and 30 are directed to an isolated Cadherin-like asymmetry protein-3 (CLASP-3) polynucleotide wherein the polynucleotide is (a) a polynucleotide that has the sequence of SEQ ID NO: 1, (b) a polynucleotide that hybridizes under stringent hybridization conditions to (a) and encodes a polypeptide having the sequence of SEQ ID NO: 2 or an allelic

variant or homologue, (c) a polynucleotide that hybridizes under stringent hybridization conditions to (a) and encodes a polypeptide with at least 25 contiguous residues of the polypeptide of SEQ ID NO: 2, or (d) a polynucleotide that hybridizes under stringent hybridization conditions to (a) and has at least 12 contiguous bases identical to or exactly complementary to SEQ ID NO: 1. The claims further recite that the polynucleotide encodes a polypeptide having the sequence of SEQ ID NO: 2. The claims recite an isolated CLASP-3 polynucleotide comprising a nucleotide sequence that has at least 90% identity to SEQ ID NO: 1. The claims also recite an expression vector comprising the polynucleotide, a host cell, and a method for producing the polypeptide. Additionally, the claims are directed to an antisense oligonucleotide complementary to a mRNA comprising SEQ ID NO: 1 and an antisense polynucleotide less than about 200 bases in length. The claims recite a pharmaceutical composition comprising a polynucleotide and a pharmaceutically acceptable carrier.

The specification asserts that the CLASP-3 polynucleotide (SEQ ID NO:1) and polypeptide (SEQ ID NO: 2) of the present invention are involved in a variety of cellular processes, particularly related to immune function, T cell activation, regulation of T cell and B cell interactions, and in the organization, establishment, and maintenance of the "immunological synapse" (including signal transduction, cytoskeletal interactions, and membrane organization) (pg 18, lines 27-32; pg 19, lines 1-2). The specification also discloses that the CLASP-3 protein is believed to be a component of the lymphocyte organelle called the "immune gateway" that creates a docking site or portal for cell-cell contact during antigen presentation (pg 19, lines 3-12). However, the instant specification does not teach any significance or functional characteristics of the CLASP-3 polynucleotide (SEQ ID NO: 1) or polypeptide (SEQ ID NO: 2).

The specification also does not disclose any methods or working examples that indicate the polynucleotide and polypeptide of the instant invention are involved in any of the abovementioned activities. Since significant further research would be required of the skilled artisan to determine how the claimed polypeptide is involved with the above-mentioned activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed putative polynucleotide (SEQ ID NO: 1):

1) to detect the expression of CLASP-3 in cells (pg 43, lines 14-16; pg 49-52; pg 77-79)

2) in the diagnosis of a disorder or disease resulting from aberrant expression of CLASP-3 (pg 43, lines 16-32)

3) as hybridization probes for cDNA and genomic DNA (pg 44-45; pg 46, lines 1-8)

4) as primers for a nucleic acid amplification (pg 44-45, pg 46, lines 1-8)

5) to treat, detect, or modulate immune system disorders, hematopoietic cell disorders, allergic reactions, organ rejection or graft-versus-host disease, inflammation, infectious agents (pg 46-48)

6) to engineer hammerhead motif ribozyme molecules (pg 56, lines 28-24; pg 57, lines 1-9)

7) for gene therapy (pg 58, lines 26-32; pg 59-62)

8) to construct a transgenic animal (pg 63-64, lines 1-19)

9) in chromosome mapping (pg 64, lines 20-34; pg 65-66)

10) to screen CLASP-3 agonists and antagonists (pg 42, lines 17-18)

Each of these shall addressed in turn.

1) to detect the expression of CLASP-3 in cells. This asserted utility is credible, but not specific or substantial. The specification does not disclose a specific target sequence. The specification does not disclose the cell types that express CLASP-3. Significant further experimentation would be required of the skilled artisan to identify cells with CLASP-3. Since this asserted utility is also not present in mature form so that it could be readily used in real world sense, the asserted utility is not substantial.

2) in the diagnosis of a disorder or disease resulting from aberrant expression of CLASP-3. This asserted utility is credible but not specific or substantial. The specification does not disclose disorders associated with a mutated, deleted, or translocated CLASP-3 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not present in mature form so that it could be readily used in real world sense, the asserted utility is not substantial.

3) as hybridization probes for cDNA and genomic DNA. This asserted utility is credible but not substantial or specific. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) as primers for a nucleic acid amplification. This asserted utility is credible but not substantial or specific. Primers can be designed from any polynucleotide sequence. Further, the specification does not disclose a specific DNA target. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) to treat, detect, or modulate immune system disorders, hematopoietic cell disorders, allergic reactions, organ rejection or graft-versus-host disease, inflammation, infectious agents. This asserted utility is credible but not specific or substantial. The specification does not disclose disorders associated with a mutated, deleted, or translocated CLASP-3 gene (SEQ ID NO: 1). The specification does not disclose which disorders are associated with altered levels of the CLASP-3 gene. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6) to engineer hammerhead motif ribozyme molecules. This asserted utility is credible but not specific or substantial. Ribozymes can be designed from any DNA/RNA sequence. Additionally, the specification does not disclose a specific DNA/RNA target. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

7) for gene therapy. This asserted utility is not credible, specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated CLASP-3 gene of SEQ ID NO: 1. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

8) to construct a transgenic animal. This asserted utility is credible but not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or

translocated CLASP-3 gene (SEQ ID NO: 1). Significant further experimentation would be required of the skilled artisan to identify such a disease. The specification discloses nothing about whether the gene will be "knocked in" or "knocked out" or what specific tissues and cells are being targeted. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

9) in chromosome mapping. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification does not disclose a specific DNA target. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

10) to screen CLASP-3 agonists and antagonists. This asserted utility is credible but not specific or substantial. Such assays can be performed with any polynucleotide. Nothing is disclosed about how the polynucleotide is affected by the compounds. Additionally, the specification discloses nothing specific or substantial for the CLASP-3 agonists and antagonists screened in this method. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

7. Claims 1-6, 8-17, and 32 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Furthermore, claims 1-4, 6-11, 14-15, and 30 recite a CLASP-3 polynucleotide wherein the polynucleotide is a polynucleotide that hybridizes under stringent hybridization conditions to

(a) and encodes a polypeptide having the sequence of SEQ ID NO: 2 or an allelic variant or homologue, a polynucleotide that hybridizes under stringent hybridization conditions to (a) and encodes a polypeptide with at least 25 contiguous residues of the polypeptide of SEQ ID NO: 2, or (d) a polynucleotide that hybridizes under stringent hybridization conditions to (a) and has at least 12 contiguous bases identical to or exactly complementary to SEQ ID NO: 1. The claims also recite an isolated CLASP-3 polynucleotide comprising a nucleotide sequence that has at least 90% identity to SEQ ID NO: 1. Additionally, the claims are directed to an antisense polynucleotide less than about 200 bases in length.

The specification discloses that "the CLASP-3 variants of the invention can contain alterations in the coding regions, non-coding regions, or both" (pg 40, lines 1-2). The specification teaches that known methods of protein engineering and recombinant DNA technology can generate variants to improve or alter the characteristics of the CLASP-3 polypeptides (pg 40, lines 25-27). However, the specification does not teach any allelic variants or homologs of the CLASP-3 polynucleotide or polypeptide. The specification does not disclose (i) a polynucleotide that encodes a polypeptide with at least 25 contiguous residues of the polypeptide of SEQ ID NO: 2, (ii) a polynucleotide that has at least 12 contiguous bases identical to or exactly complementary to SEQ ID NO: 1, or (iii) an antisense polynucleotide less than about 200 bases in length. The specification also does not teach a nucleic acid sequence with 90% sequence identity to the nucleotide sequence of SEQ ID NO: 1. Furthermore, regarding allelic variants, it is noted that such are recognized in the art as variant genes which map to the same locus on the chromosome (See Lewin, Genes II, 1985, pg 681). The specification does not disclose the chromosomal location of any of CLASP-3 gene characterized by the inventors.

Additionally, the specification does not teach functional or structural characteristics of any polynucleotide variants in the context of a cell or organism.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small

domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotide to make biologically active CLASP-3 without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding CLASP-3 for purposes unrelated to the asserted biological activity. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polynucleotide encoding CLASP-3 could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

Further, the problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. For example, while it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also

be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein and DNA which are tolerant to change and the nature and extent of changes that can be made in these positions. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Furthermore, claim 30 is directed to a pharmaceutical composition comprising a CLASP-3 polynucleotide and a pharmaceutically acceptable carrier. The specification teaches a composition comprising an isolated CLASP-3 polynucleotide consisting of the nucleic acid sequence of SEQ ID NO: 1. The specification does not teach how to use a CLASP-3 "pharmaceutical" composition and a "pharmaceutically acceptable carrier" without undue experimentation for the treatment of a disease in an animal. The specification lists disorders to be treated (pg 49-54), but there are no working examples directed to a particular disorder in an animal or administration of the CLASP-3 polynucleotide consisting of the nucleic acid sequence of SEQ ID NO: 1 to an animal for treatment. (Note, this issue could be overcome by deleting the terms "pharmaceutical" and "pharmaceutically acceptable" from the claims.)

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding CLASP-3, to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, and to determine the quantity of CLASP-3 polynucleotide to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding same and the lack of direction/guidance presented in the specification regarding the chromosomal locus of the CLASP-3 gene disclosed in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, the unpredictability of the effects of the CLASP-3 polynucleotide *in vivo* and the unpredictable nature of the locus for any isolated gene, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural fragments and variants and which recite any allelic variant, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

9. Claims 1-4, 6-11, 14-15, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, claims 1-4, 6-11, 14-15, and 30 are directed a CLASP-3 polynucleotide wherein the polynucleotide is a polynucleotide that hybridizes under stringent hybridization conditions to (a) and encodes a polypeptide having the sequence of SEQ ID NO: 2 or an allelic variant or homologue, a polynucleotide that hybridizes under stringent hybridization conditions to (a) and encodes a polypeptide with at least 25 contiguous residues of the polypeptide of SEQ ID NO: 2, or (d) a polynucleotide that hybridizes under stringent hybridization conditions to (a) and has at least 12 contiguous bases identical to or exactly complementary to SEQ ID NO: 1. The claims also recite an isolated CLASP-3 polynucleotide comprising a nucleotide sequence that has at least 90% identity to SEQ ID NO: 1. Additionally, the claims are directed to an antisense polynucleotide less than about 200 bases in length.

The specification teaches human a CLASP-3 polynucleotide and polypeptide (SEQ ID NO: 1 and SEQ ID NO: 2, respectively). The specification also discloses that "the CLASP-3 variants of the invention can contain alterations in the coding regions, non-coding regions, or both" (pg 40, lines 1-2). The specification teaches that known methods of protein engineering and recombinant DNA technology can generate variants to improve or alter the characteristics of the CLASP-3 polypeptides (pg 40, lines 25-27). However, the specification does not teach functional or structural characteristics of the polynucleotide variants in the context of a cell or organism. The description of one CLASP-3 polynucleotide species (SEQ ID NO: 1) and one CLASP-3 polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants and fragments (i) with at least 90% sequence identity to the human CLASP-3 polynucleotide comprising SEQ ID NO: 1. The description of one CLASP-3 polynucleotide species and one

CLASP-3 polypeptide species is also not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants and fragments (ii) that encode a polypeptide with at least 25 contiguous residues, (iii) have at least 12 bases identical to or exactly complementary to SEQ ID NO: 1, and (iv) have antisense polynucleotide less than 200 bases in length.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated CLASP-3 polynucleotide that has the nucleotide sequence of SEQ ID NO:1 or a CLASP-3 polynucleotide that encodes a polypeptide having the sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

10. Claim 3 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The invention appears to employ novel nucleic acid molecules (i.e., clones AVC-PD3, AVC-PD9, AVC-PD21, AVC-PD22). Since the nucleic acid molecules are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the nucleic acid molecules are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the nucleic acid molecules. The specification does not disclose a repeatable process to obtain the nucleic acid molecules and it is not apparent if the nucleic acid molecules are readily available to the public. It is noted that Applicant has deposited the nucleic acid molecules (p. 108 of the specification), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the

nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include such, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 6-11, 14-15, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al. (Genbank Accession No. AA429436; 16 October 1997) in view of Sibson et al. (WO 94/01548).

Hillier et al. teach an isolated polynucleotide that has at least 12 contiguous bases identical to or exactly complementary to SEQ ID NO: 1 of the instant application and an antisense polynucleotide less than 200 bases in length (See sequence alignment attached to this Office Action as Appendix A; see nucleotides 1-588 of Hillier et al.; see nucleotides 744-1331 of SEQ ID NO: 1 of the instant application, for example).

Hillier et al. does not teach expression vectors, host cells, or a method of producing a polypeptide.

Sibson et al. discloses that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein (see pages 8-13).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use Hillier's DNA and the expression vector, host cell, and method of expressing and then isolating the encoded polypeptide as taught by Sibson et al. in view of Sibson's suggestion that it would be desirable to do so, as cited above.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB
Art Unit 1647
August 2, 2002

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER